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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/522,716	03/10/2000	Edward P. Cohen	10464A	6035

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EXAMINER
YAEN, CHRISTOPHER H

ART UNIT	PAPER NUMBER
1642	14

DATE MAILED: 04/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/522,716	COHEN, EDWARD P.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 January 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26 and 41-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26 and 41-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The amendment after final filed 1/06/2003 (paper no 13) is acknowledged and entered into the record. Upon further review and reconsideration, the finality of the instant application is withdrawn.

2. All rejections of prior office actions are also withdrawn, and new grounds of rejection will be applied.

3. Currently, claims 26, 41-46 are pending and examined on the record.

Claim Rejections - 35 USC § 112,2nd paragraph

4. Claims 26, 41-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. With regard to claims 26 and dependent claims thereof in the recitation of the term "effective amount", it is unclear from the specification as to the quantity needed to effectively inhibit tumors. The specification has not defined this amount.

6. With regard to claim 26 and dependent claims thereof, it is not clear as to whether the tumor referred is present prior to the administration of the MHC-1 expressing cells.

7. With regard to claims 26 and dependent claims thereof in the recitation of the term "determinant", the specification has not adequately defined this term. Does the applicant intend for the determinant to be a receptor?

8. With regard to claim 26 and dependent claims thereof in the recitation of the term "genomic DNA", the intended DNA referred is not adequately defined. As such the metes and bounds cannot be determined.

Claim Rejections - 35 USC § 112,1st paragraph

9. Claims 26 and 41-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating the growth of a tumor cell in a subject comprising the administration of an antigen presenting cell expressing a syngeneic MHC I molecule, an allogeneic MHC I molecule, IL-2, and genomic DNA isolated from a tumor to which treatment is being applied, does not reasonably provide enablement for a method of preventing a tumor in a subject comprising the administration of an antigen presenting cell expressing syngeneic MHC II molecules, allogenic MHC II molecules, any and all cytokines, and genomic DNA from tumors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The claims of the instant invention are drawn to a method of preventing or treating a tumor in an animal comprising the administration of an antigen presenting cell expressing a syngeneic MHC I or II molecule, an allogeneic MHC I or II molecule, a cytokine, and genomic DNA isolated from tumor cells of said animal. The specification discloses the transformation of an LM cell (a fibroblast cell lines) expressing a MHC class I molecule H-2^K with a vector encoding an IL-2 molecule, thereby generating the new cell line LM-IL-2. The specification also details the further transformation of this

cell, LM-IL-2, with an additional MHC class I molecule, H-2K^b, thereby generating the semi-allogeneic antigen presenting cell, LM-IL-2K^b. And lastly, the specification teaches the transformation of the LM-IL-2K^b with genomic DNA isolated from the tumor of the animal, and the subsequent administration and inhibition of tumor growth in the animal. However, nowhere in the specification does it teach a method of administering to an animal a semi-allogenic antigen presenting cell comprising MHC class II molecules that are either syngeneic or allogeneic. Furthermore, the specification has not taught cytokines other than IL-2. And further still, the specification is devoid of teaching a method of preventing a tumor.

It is a well established fact that the structure and function of the MHC class I and II molecules are very different and distinct (see Roitt *et al* Immunology 4th ed. 1998; see pgs 11.7-11.14 for review). Such differences exist in the types of T-cell response generated from the MHC molecules, and the size of the peptide that is able to bind within the binding pocket. As such, one of skill in the art has only been taught how an animal is to respond with a semi-allogeneic cell expressing MHC class I molecules. The type of T-cell response may be critical for the total understanding of the practice of the invention. Currently, the artisan has only really been taught how CD8 cells respond to the presence of the semi-allogeneic antigen presenting cell. To determine how and what function a CD4 cell response might have on tumor cell prevention or inhibition would require a large amount of experimentation by the skilled artisan.

It is also a well established fact, that the introduction of different cytokines to a system will generate different types of immune responses (see Lappin MB *et al* Blood

Reviews 2000 14:228-239 for review) . Currently, the instant specification has only provided the artisan with effects of the administration of IL-2 in inhbition of tumor cell growth. This cytokine is seen as a broad immune cell mediator generating both TH1 and TH2 type immune responses. Because the type of immune response is critical for the inhibition of tumor cell growth, one of skill in the art would be subject to a large amount of experimentation to determine the effects other cytokines may have on the inhibition of tumors. The specification specifically states that certain cytokines, namely IL-2 at high doses becomes toxic (see page 4). The specification further states that the role of cytokines in the inhibition of tumor is to modulate different immunological responses, but the skilled artisan in this instant case has only been taught one type of response generated. As such the skilled artisan would be forced into large amount of experimentation to determine what effect the administration of other cytokines would have on the system.

And lastly, it is a well established fact that the treatment of cancer is unpredictable and difficult, and that the pre-emptive treatment or prevention of cancer is difficult because current technologies prevent us from pre-determining which patients should be subject to treatment (see Evan *et al*). It is noted that the specification does in fact teach the inhibition of tumor growth when semi-allogeneic antigen presenting cell were administered prior to the challenge of tumor cells. However, this does not entitle the applicant to a method of preventing a tumor because the phrase preventing a tumor indicates an infinite blockade of tumor growth that is boundless in time. The administration or challenge of a tumor 150 days following administration is not clear

indication that a tumor is clearly prevented. Furthermore, it is not clear how a tumor that is administered is actually prevented because when a tumor in the instant specification was administered, it was not actually prevented, but it was in fact inhibited from growing and establishing.

Therefore, given the apparent lack of an enabling disclosure as it pertains to the prevention of tumors, the use of MHC class II molecules, and the use of any and all cytokines, one of skill in the art would be forced into undue experimentation to practice the instant invention.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 26, 41, 42, and 44-45 rejected under 35 U.S.C. 102(b) as being anticipated by Eisenbach L *et al* (EP 0 569 678 A2). Claims are drawn to a method of treating or preventing an tumor in an animal comprising the administration of an antigen presenting cell that expresses syngeneic and allogeneic MHC molecules and genomic DNA isolated from the tumor of said animal. The claims are further limited to a tumor being selected from a group of which includes lung cancer, and further comprising an IL-2 cytokine. Eisenbach *et al* disclose a method of treating a tumorous diseases, which include lung cancer, with a tumor cell expressing both a syngeneic and allogenic MHC molecule. Eisenbach *et al* also disclose of using cytokines such as IL-2 (see page 4).

Because the cell used is a tumor cell, it inherently has within it and expresses its own genomic DNA. Furthermore, the claim is given its broadest interpretation and therefore, because tumor cells have tumor associated antigens associated with it surface repertoire and because when administered to a subject would in fact present its antigen, it is also considered to an antigen presenting cell.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

13. Claims 26, 41, 42, and 44-45 are rejected under 35 U.S.C. 102(e) as being anticipated by Eisenbach *et al* (5,750,102; 05/1998). Claims are drawn to a method of treating or preventing an tumor in an animal comprising the administration of an antigen presenting cell that expresses syngeneic and allogeneic MHC molecules and genomic DNA isolated from the tumor of said animal. The claims are further limited to a tumor being selected from a group of which includes lung cancer, and further comprising an IL-2 cytokine. Eisenbach *et al* disclose a method of treating a tumorous diseases, which include lung cancer, with a tumor cell expressing both a syngeneic and allogenic MHC molecule. Eisenbach *et al* also disclose of using cytokines such as IL-2 (see

column 4). Because the cell used is a tumor cell, it inherently has within it and expresses its own genomic DNA. Furthermore, the claim is given its broadest interpretation and therefore, because tumor cells have tumor associated antigens associated with it surface repertoire and because when administered to a subject would in fact present its antigen, it is also considered to an antigen presenting cell.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 703-305-3586. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Christopher Yaen
Art Unit 1642
April 6, 2003

PRIMARY EXAMINER
ALI R. SALIMI